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STN Express with Discover!
NEWS 11 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 12 SEP 14 STN Patent Forum to be held October 13, 2004, in Iselin, NJ
NEWS 13 SEP 27 STANDARDS will no longer be available on STN
NEWS 14 SEP 27 SWETSCAN will no longer be available on STN

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 19:26:58 ON 12 OCT 2004

=> FIL STNGUIDE

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

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FILE CONTAINS CURRENT INFORMATION.
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=> file caplus	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.06	0.27

FILE 'CAPLUS' ENTERED AT 19:27:35 ON 12 OCT 2004
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FILE COVERS 1907 - 12 Oct 2004 VOL 141 ISS 16
FILE LAST UPDATED: 11 Oct 2004 (20041011/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s ascorbic acid
      76036 ASCORBIC
      3880255 ACID
      1449056 ACIDS
      4351117 ACID
            (ACID OR ACIDS)
L1      75366 ASCORBIC ACID
            (ASCORBIC(W) ACID)

=> s l1 and lysine or proline
      95574 LYSINE
      1978 LYSINES
      96175 LYSINE
            (LYSINE OR LYSINES)
      61133 PROLINE
      1070 PROLINES
      61458 PROLINE
            (PROLINE OR PROLINES)
L2      62122 L1 AND LYSINE OR PROLINE

=> s l2 and composition
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      277266 COMPOSITIONS
      893281 COMPOSITION
            (COMPOSITION OR COMPOSITIONS)
      1299928 COMPN
      521505 COMPNS
      1591699 COMPN
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(COMPN OR COMPNS)
2027094 COMPOSITION
(COMPOSITION OR COMPN)

L3 9378 L2 AND COMPOSITION

=> s l3 and covalent bond
54216 COVALENT
8 COVALENTS
54218 COVALENT
(COVALENT OR COVALENTS)
490962 BOND
246787 BONDS
633432 BOND
(BOND OR BONDS)
9195 COVALENT BOND
(COVALENT(W) BOND)

L4 8 L3 AND COVALENT BOND

=> d l4 ibib hitstr abs 1-8

L4 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:220329 CAPLUS

DOCUMENT NUMBER: 140:270870

TITLE: Preparation of quinazolinone derivatives as inosine
5'-monophosphate dehydrogenase inhibitors with
therapeutic uses

INVENTOR(S): Haughan, Alan Findlay; Buckley, George Martin; Davies,
Natasha; Dyke, Hazel Joan; Hannah, Duncan Robert;
Morgan, Trevor; Richard, Marianna Dilani; Sharpe,
Andrew; Williams, Sophie Caroline

PATENT ASSIGNEE(S): Celltech R & D Limited, UK

SOURCE: PCT Int. Appl., 102 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022554	A1	20040318	WO 2003-GB3878	20030905
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.:

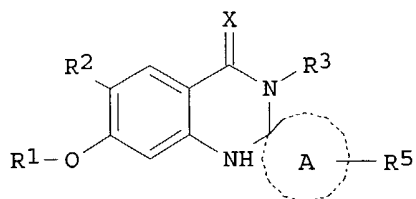
GB 2002-20813 A 20020907

GB 2002-29186 A 20021214

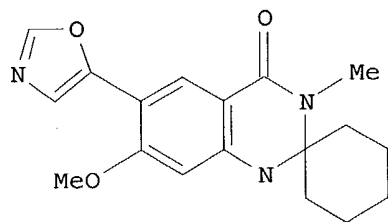
GB 2003-12775 A 20030604

OTHER SOURCE(S): MARPAT 140:270870

GI



I



II

AB Quinazolinones and quinazolinethiones (shown as I; variables defined below; e.g. II) and the salts, solvates, hydrates, tautomers, isomers or N-oxides thereof are claimed. Compds. I are potent inhibitors of IMP dehydrogenase (IMPDH); each of the 118 examples inhibit IMPDH with IC50 ≤5 μM. For I: X is O or S; R1 is an aliphatic, cycloaliph. or cycloalkyl-alkyl-; R2 is an (un)substituted heteroarom. group or a -CN group; R3 is -(Alk1)mL1(Alk2)nR4 (m and n are each 0 or 1; Alk1 and Alk2 are each an (un)substituted aliphatic or heteroaliph. chain; L1 is a **covalent bond** or a linker atom or group; and R4 is H or an (un)substituted cycloaliph., heterocycloaliph., aromatic or heteroarom. group). A is an (un)substituted cycloaliph. or heterocycloaliph. group optionally fused to an (un)substituted aryl or heteroaryl group; R5, which may be attached to any available C or N atom present in the cycloaliph. or heterocycloaliph., or where fused, aryl or heteroaryl group, is a group -(Alk3)tL2(Alk4)vR6 (t and v are each 0 or 1; Alk3 and Alk4 are each an (un)substituted aliphatic or heteroaliph. chain; L2 is a **covalent bond** or a linker atom or group; and R6 is a H or halogen atom or a -CN group or an (un)substituted cycloaliph., heterocycloaliph., aromatic or heteroarom. group). Although the methods of preparation are not claimed, 118 example preps. are included. For example, II was prepared in 60 % yield from 2-amino-4-methoxy-N-methyl-5-(oxazol-5-yl)benzamide, MgSO4 and PTSA in CH2Cl2 to which cyclohexanone was added.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:444425 CAPLUS

DOCUMENT NUMBER: 137:17443

TITLE: Affinity labeling libraries with tagged leaving group

INVENTOR(S): Krantz, Alexander; Hanel, Arthur M.; Huang, Wolin

PATENT ASSIGNEE(S): Conjuchem Inc., Can.

SOURCE: U.S., 11 pp., Cont.-in-part of U.S. Ser. No. 714,754, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6403324	B1	20020611	US 1998-42234	19980313
PRIORITY APPLN. INFO.:			US 1996-714754	B2 19960916
OTHER SOURCE(S):		MARPAT 137:17443		

AB Methods and **compns.** are provided for identifying compds. having affinity to a target site. The method provides for the affinity group to be a leaving group from a reactive functionality capable of forming a **covalent bond** to the target site. One can combine the compound comprising the target site with the library, and assay for the resulting **compn.** of the leaving groups. The leaving groups having the highest concentration can be identified as the groups having the binding highest affinity for the target site. The selected compds. may then be used for labeling the target mol., particularly where the target mol. is naturally found in a complex mixture, such as a physiol. fluid, like blood. By affinity labeling in vivo, the lifetime of physiol. active entities can be greatly enhanced by becoming bound to long lived blood components. The covalently bound entity may also serve as an antagonist or agonist of particular binding proteins or as an enzyme inhibitor. An affinity labeling peptide library with tagged leaving groups and having a p-thiobenzoic acid residue as a separator was designed and constructed.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:798225 CAPLUS

DOCUMENT NUMBER: 135:344471

TITLE: Preparation of diazabicyclic compounds as central nervous system active agents

INVENTOR(S): Schrimpf, Michael R.; Tietje, Karin R.; Toupence, Richard B.; Ji, Jianguo; Basha, Anwer; Bunnelle, William H.; Daanen, Jerome F.; Pace, Jennifer M.; Sippy, Kevin B.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 190 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

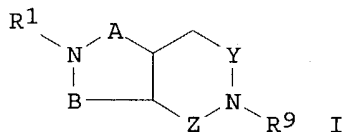
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081347	A2	20011101	WO 2001-US13798	20010427
WO 2001081347	A3	20020131		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002019388	A1	20020214	US 2001-833914	20010412
BR 2001007246	A	20021001	BR 2001-7246	20010427
EP 1284976	A2	20030226	EP 2001-944118	20010427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531210	T2	20031021	JP 2001-578437	20010427
ZA 2002008274	A	20040211	ZA 2002-8274	20021014
NO 2002005107	A	20021219	NO 2002-5107	20021024
BG 107303	A	20030731	BG 2002-107303	20021121
US 2004186107	A1	20040923	US 2004-810999	20040326
PRIORITY APPLN. INFO.:				
			US 2000-200111P	P 20000427
			US 2000-559943	A 20000427
			US 2001-833914	A 20010412
			WO 2001-US13798	W 20010427

OTHER SOURCE(S): MARPAT 135:344471

GI



AB Diazabicyclic compds. (I; e.g. cis-2-(3-pyridinyl)octahydropyrrolo[3,4-c]pyrrole dihydrochloride), pharmaceutical **compns.** of these compds., and use of said **compns.** to control synaptic transmission in mammals are claimed. In I: A = **covalent bond**, CH₂, CH₂CH₂, and CH₂CH₂CH₂; B = CH₂ and CH₂CH₂, provided that when A is CH₂CH₂CH₂, then B is CH₂; Y = **covalent bond**, CH₂, and CH₂CH₂; Z = **covalent bond**, CH₂, and CH₂CH₂, provided that when Y is CH₂CH₂, then Z is a **covalent bond** and further provided that when Z is CH₂CH₂, then Y is a **covalent bond**. R₁ = optionally substituted phthalazin-1-yl, pyridin-3-yl, pyrazinyl, pyrimidin-5-yl, pyridazin-3-yl, quinolin-3-yl, thieno[3,2-b]pyridin-2-yl, furano[3,2-b]pyridin-2-yl, thieno[3,2-b]pyridin-3-yl, furano[3,2-b]pyridin-3-yl, furano[3,2-b]pyridin-6-yl, thieno[3,2-b]pyridin-6-yl, furano[2,3-b]pyridin-5-yl, thieno[2,3-b]pyridin-5-yl, isothiazol-5-yl, isoxazol-5-yl. R₉ = H, alkoxycarbonyl, alkyl, amino, aminoalkyl, aminocarbonylalkyl, benzyloxycarbonyl, cyanoalkyl, dihydro-3-pyridinylcarbonyl, hydroxy, hydroxyalkyl, and phenoxycarbonyl. Values are reported for nicotinic acetylcholine receptor binding potencies and effectiveness of nicotinic acetylcholine receptor ligands as analgesic agents and in the formalin test for some of the claimed compds. Ninety-six example prepns. are given but the methods of preparation are not claimed. The crystal and mol. structures of (3aS,6aS)-5-[(4-nitrophenyl)sulfonyl]-1-((1R)-1-phenylethyl)octahydropyrrolo[3,4-b]pyrrole and tert-Bu (3S,4S)-4-(hydroxymethyl)-3-[(1S)-1-phenylethylamino]-1-piperidinecarboxylate were determined by x-ray crystallog.

L4 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1998:388485 CAPLUS
 DOCUMENT NUMBER: 129:51430
 TITLE: Aminoguanidine and alkoxyguanidine protease inhibitors, method for their synthesis and pharmaceutical use
 INVENTOR(S): Tomczuk, Bruce E.; Soll, Richard M.; Lu, Tianbao; Fedde, Cynthia L.; Illig, Carl R.; Markotan, Thomas P.; Stagnaro, Thomas P.
 PATENT ASSIGNEE(S): 3-Dimensional Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 191 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9823565	A2	19980604	WO 1997-US21649	19971126
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,				

GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

TW 499412	B	20020821	TW 1997-86117721	19971125
CA 2273023	AA	19980604	CA 1997-2273023	19971126
AU 9854584	A1	19980622	AU 1998-54584	19971126
AU 725058	B2	20001005		
ZA 9710646	A	19980915	ZA 1997-10646	19971126
EP 944590	A2	19990929	EP 1997-948537	19971126
EP 944590	B1	20020320		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI

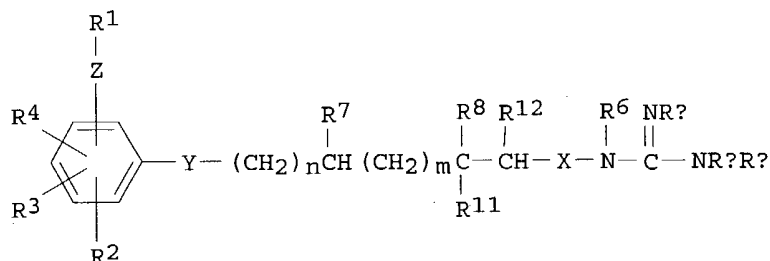
CN 1237961	A	19991208	CN 1997-199940	19971126
BR 9713328	A	20000509	BR 1997-13328	19971126
JP 2001506606	T2	20010522	JP 1998-524829	19971126
US 6235778	B1	20010522	US 1997-979234	19971126
AT 214693	E	20020415	AT 1997-948537	19971126
ES 2174309	T3	20021101	ES 1997-948537	19971126
NO 9902512	A	19990726	NO 1999-2512	19990525
MX 9904889	A	20000630	MX 1999-4889	19990526
US 6638931	B1	20031028	US 2000-722363	20001128
US 2001037039	A1	20011101	US 2001-809293	20010316
US 6518310	B2	20030211		
US 2003158252	A1	20030821	US 2003-359078	20030206
US 6706765	B2	20040316		
US 2004002539	A1	20040101	US 2003-419972	20030422
US 6730783	B2	20040504		

PRIORITY APPLN. INFO.:

US 1996-31822P	P	19961126
US 1997-979234	A3	19971126
WO 1997-US21649	W	19971126
US 2000-722363	A3	20001128

OTHER SOURCE(S): MARPAT 129:51430

GI



I

AB Aminoguanidine and alkoxyguanidine compds. (I; X=O, NR⁹; Y=O, NR¹⁰, S, CHR¹⁰, **covalent bond**; Z=NR¹⁰SO₂, SO₂NR¹⁰, NR¹⁰C(R_yR_z), C(R_yR_z)NR¹⁰, OSO₂, SO₂O, OC(R_yR_z), C(R_yR_z)O, NR¹⁰CO, CONR¹⁰; R¹-R⁴, R⁶-R¹²=alkyl, etc.; R_a, R_b, R_c=H, OH, CN, CO₂R_w, alkyl, alkoxy, aryloxy, aralkoxy, alkoxy-carbonyloxy; R_w=alkyl, cycloalkyl, Ph, benzyl, etc.; R_y, R_z=H, alkyl, cycloalkyl, aryl, aralkyl, hydroxyalkyl, carboxyalkyl, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, carboxy; n=0-8; m=0-4) as well as hydrates, solvates or pharmaceutically acceptable salts thereof, that inhibit proteases are described. Also described are methods for preparing I involving reaction of an aminoguanidine with a carbonyl compound or reaction of an alkoxyamine compound with a guanidinylation agent. The novel compds. of the present invention are potent inhibitors of proteases, especially trypsin-like serine proteases, such as chymotrypsin, trypsin, thrombin, plasmin and factor Xa. Certain of the compds. exhibit antithrombotic activity via direct, selective inhibition of thrombin, or

are intermediates useful for forming compds. having antithrombotic activity. The invention includes a **compn.** for inhibiting loss of blood platelets, inhibiting formation of blood platelet aggregates, inhibiting formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation in a mammal, comprising a compound of the invention in a pharmaceutically acceptable carrier. Other uses of compds. of the invention are as anticoagulants either embedded in or phys. linked to materials used in the manufacture of devices used in blood collection, blood circulation, and blood storage, such as catheters, blood dialysis machines, blood collection syringes and tubes, blood lines and stents. A large number of I were prepared and tested for inhibition of proteases. Seven compds. displayed Ki 2.6-11 nM for thrombin.

L4 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:387760 CAPLUS
DOCUMENT NUMBER: 129:108160
TITLE: Salt-soluble seed globulins of various dicotyledonous and monocotyledonous plants - I.
Isolation/purification and characterization
AUTHOR(S): Marcone, Massimo F.; Kakuda, Yukio; Yada, Rickey Y.
CORPORATE SOURCE: Department of Food Science, Univ. of Guelph, Guelph, ON, N1G 2W1, Can.
SOURCE: Food Chemistry (1998), 62(1), 27-47
CODEN: FOCHDJ; ISSN: 0308-8146
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Detailed characterization of 21 purified seed globulins derived from both monocotyledonous and dicotyledonous plants indicated that globulins from both class types (as well as within the same class type) lay within a narrow mol. weight range between 300,000 and 370,000 Da and were composed of multiple subunits. In all cases, purified globulins could be classified as hetero-oligomers being composed of a non-equimolar ratio of various subunits. The vast majority of subunits forming these globulins were shown to be held together by non-covalent bond forces. A small percentage of linkages between subunits were also shown to be disulfide linked, in the case of dicotyledonous seed globulins. It was also found that the majority of subunits composing the dicotyledonous and monocotyledonous seed globulins examined fell within two very narrow mol. weight ranges, i.e. 20,000-27,000 and 30,000-39,000 Da and were believed to correspond to basic and acidic subunits, resp. Unlike monocotyledonous seed globulins, globulins derived from dicotyledonous plants were found to undergo alkaline-induced dissociation due to electrostatic repulsion between subunits. The amino acid **compn.** of both dicotyledonous and monocotyledonous seed globulins suggests that they have a storage role and may be similar proteins based on a high content of amides (glutamic acids-glutamine and aspartic acid-asparagine and arginine). From the results of the structural and chemical data obtained in this study, it is concluded that the 11S storage globulin, having several similar properties, exists in many leguminous and nonleguminous dicotyledonous plants as well as monocotyledonous plants. This similarity among 11S storage globulins could be due either to convergent evolution in response to a common functional need, or to common ancestry.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1987:642444 CAPLUS
DOCUMENT NUMBER: 107:242444
TITLE: Proteolipids, their use as humectants, and measurement of their humectancy
INVENTOR(S): Schiltz, John R.; Elias, Peter M.
PATENT ASSIGNEE(S): American Cyanamid Co., USA
SOURCE: Eur. Pat. Appl., 17 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 228711	A2	19870715	EP 1986-118139	19861230
EP 228711	A3	19890419		
R: BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4792571	A	19881220	US 1986-815491	19860102
DK 8606341	A	19870703	DK 1986-6341	19861230
NO 8605358	A	19870703	NO 1986-5358	19861230
JP 62223198	A2	19871001	JP 1986-315979	19861230
ZA 8609774	A	19871028	ZA 1986-9774	19861230
FI 8605367	A	19870703	FI 1986-5367	19861231
AU 8667099	A1	19870709	AU 1986-67099	19861231
PRIORITY APPLN. INFO.:			US 1986-815481	19860102
			US 1986-815482	19860102
			US 1986-815483	19860102
			US 1986-815491	19860102

AB Proteolipids, with a **covalent bond** between the protein and lipid components, are used as humectants for skin and hair. The comparative humectancy of materials is determined by a) drying the material b) allowing the material to absorb radioactive water vapor and c) measuring the radioactivity of the material. Murine epidermal proteolipids adsorbed 119.8 µg H₂O/µg proteolipids, whereas hyaluronic acid and neutral lipid mixture adsorbed 19.7 and 31.7 µg H₂O/µg material, resp. In humans at 0.5% bovine proteolipids increased the rate of hydration of the stratum corneum faster than water. The humectant proteolipids gradually increased the water content until at 6 h the water content of the skin was equivalent to that of skin treated with petrolatum.

L4 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1981:98500 CAPLUS
DOCUMENT NUMBER: 94:98500
TITLE: Characterization of **proline** endopeptidase from rat brain
AUTHOR(S): Andrews, Philip C.; Hines, Catherine M.; Dixon, Jack E.
CORPORATE SOURCE: Dep. Biochem., Purdue Univ., West Lafayette, IN, 47907, USA
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AB A homogeneous **proline** endopeptidase from rat brain was characterized with respect to its substrate specificity and the residues essential for catalysis. The 2 fluorogenic substrate analogs tested, pyroglutamylhistidylprolyl-β-naphthylamide and pyroglutamyl-(N-benzylimidazolyl)histidylprolyl-β-naphthylamide, had higher V_{max} values (19.5 and 26.9 µmol/min/g, resp.) and considerably lower K_m values (0.034 and 0.020 mM, resp.) than pyroglutamylhistidylprolinamide (V_{max} = 2.9 µmol/min/mg and K_m = 4.1 mM). Both fluorogenic substrates gave rise to pH optima and pH rate profiles similar to those of the amide. Values of K_m and k_{cat} were determined as a function of pH. The K_m was pH-independent, with the titration curve for k_{cat}/K_m implicating an active-site residue(s) with a pK_a of 6.2. **Proline** endopeptidase could be completely inactivated by low concns. of diisopropyl fluorophosphate with an observed 2nd-order rate constant of 2.5 + 104 min/M. The stoichiometry of the alkylphosphorylation was 0.83 mol/mol enzyme. The pH dependence of the inactivation by diisopropyl fluorophosphate implicated a residue(s) involved in **covalent**

bond formation having a pKa of 6.0. Apparently, **proline** endopeptidase is a serine proteinase.

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TITLE: Secretion and extracellular processing of procollagen by cultured human fibroblasts

AUTHOR(S): Goldberg, Burton; Sherr, Charles J.

CORPORATE SOURCE: Med. Cent., New York Univ., New York, NY, USA

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AB Cultures of human diploid fibroblasts were labeled with radioactive **proline** and glycine, and the precursor of collagen (procollagen) in cells and medium was characterized by Na dodecyl sulfate-polyacrylamide gel electrophoresis. A covalently assembled mol. with the procollagen **compn.** (pro α 1)₂.pro α 2 (where pro α -1 and pro α -2 indicate addnl. N-terminal peptides on the α -1 and α -2 chains, resp.) (approx. mol. weight, 360,000) appeared intracellularly soon after synthesis of the constituent chains, and could be detected in the medium after 60 min of labeling. The mol. was stabilized by SS bonds between cysteine residues in the N-terminal procollagen peptide sequences of the 3 chains. Collagenase digested the mol. to peptides of 30,000 mol. weight or less. Limited digestion with pepsin excised nonhelical procollagen peptides, yielding native, triple-helical tropocollagen. Pulse-chase expts. indicated that a peptidase in the medium sequentially excised the nonhelical peptides from the mol., generating tropocollagen mols., that aggregated as fibers in the cell layer. The excised, nonhelical procollagen peptides contained little or no **proline** or glycine. Intramol. bonds of the lysyl aldehyde type were not detected in the secreted mol., as reduction of the medium always resulted in quant. recovery of free pro α chains in dodecyl sulfate-urea. Lysyl-derived, **covalent bonds** appeared to form between tropocollagen mols. aggregating in the cell layer. The term 'pro-tropocollagen' was suggested for the assembled, secreted precursor of collagen.